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Application No.	Ref.	Date
99 303 151.7-2117	VW/P32151	07.02.2000
Applicant: SMITHKLINE BEECHAM PLC		

Communication pursuant to Article 96(2) and Rule 51(2) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 2 months

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from the notification of this communication, this period being computed in accordance with Rules 78(3) and 83(2) and (4) EPC.

Amendments to the description, claims and drawings are to be filed where appropriate within the said period in three copies on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).

HAERTINGER S
Primary Examiner
for the Examining Division

EXR1 000207 EXR2 02M coded

Enclosure(s): : 3 page/s reasons (Form 2906)
International Journal of Pharmaceutics, 42 (1988) 135-143

Registered Letter
EPO Form 2001 10.95CSX

The examination is being carried out on the **following application documents:**

Text for the Contracting States: AT BE CH LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Description, pages:
1-49 as originally filed

Claims, No.:
1-44 as received on 04.01.2000 with letter of 23.12.1999

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1. The amendment in present claim 3 relating to the expression "treating ... an organic salt thereof" appears to embrace possibilities which go over the content of the application as filed. In particular, the new wording is neither limited to the "organic acid salt" (original claim 10) or the "salt of paroxetine with an organic acid" (page 2, lines 22-23 of the description). Accordingly, the requirements of **Art. 123(2) EPC** may not considered to have been met.

2. However, in the assumption that the applicant will overcome the above deficiency, e.g. by using one of the indicated phrases of the original disclosure, the following findings are put forward.

2.1 In view of the restrictions made the claimed subject-matter is now considered to have met the requirements of unity of invention according to Art. 82 EPC. The methanesulfonate salt of paroxetine is regarded to represent the unifying special technical feature being common to all claims.

2.2 Novelty

a) With respect to the disclosure of D1 and D2 novelty of the claimed matter resides from the above mentioned methanesulfonate ion of the paroxetin salt.

b) The international application WO-A-98 56787 (= D3), which has been cited in the European Search Report, has been published between the second priority of 06.12.98 and the third priority dated 10.02.99 of the present application. D3 has

been supplied to the EPO in one of the official languages and the national fees have been paid. The requirements of Art. 158(2) EPC are thus fulfilled. It follows from the inspection of the said priority documents that the present subject-matter of claims 1-44 is at least entitled to the said second priority. Consequently, the content of D3 as filed is considered as comprised in the state of the art relevant only to the question of novelty (Art. 54(3) and (4) EPC) for all contracting states.

D3 discloses methane sulfonate salt of paroxetine (cf. Table 1), its preparation starting from paroxetine (cf. the preparations disclosed on page 9 and in Example 1), its medical use inter alia in the treatment of depression (cf. claim 13) and its formulation into pharmaceutical compositions (cf. page 9). In view of the above disclosure, D3 appears to be a complete anticipation in the sense of Art. 54 EPC of -at least- present claims 1 (paroxetine methanesulfonate in crystalline form), 2 (preparation process), 10 (pharmaceutical composition), 19 and 36 (medical use) for the following reasons.

The table below compares the IR characteristics of paroxetine methanesulfonate as claimed in present claim 1 with (some of) the peak frequencies of the methanesulfonate salt disclosed in Table 1 of D3:

claim 1:	1599-1607;	1509-1517;	1190-1198;	1041-1049;	942-950;	826-834;
D3:	-	1515	1208	1038	931	838

cont.	claim 1:	772-780;	597-605;	550-558;	535-543		
	D3:	777	-	546	531		

The above IR data of the present compound have been obtained from measuring a nujol mull (cf. Example 2), whereas the data of D3 have been gathered from KBr discs.

However, it has been reported that the existence of two different solid state forms (at least for the hydrochloride salt of paroxetine) could hardly be analysed from IR-samples made of potassium bromide discs "... since the process of disc

preparation tended to reduce the crystallinity of both forms" (cf. results and discussion section in "International Journal of Pharmaceutics", 42, 1988, pages 135-143 & XP000572028 = D4; copy herewith). That is to say, that the mere statement that the "same characterising IR bands are found when using KBr discs" (cf. present Example 2) without giving specific evidence may not be considered as being a sufficient proof for the presence of a polymorphic form of paroxetine methanesulfonate, which were unambiguously different from that obtained by the various manufacturing processes disclosed in D3 on pages 6, 9-11. Even, if the IR data of present example 4 were compared to that disclosed in D3 (both spectra were measured in KBr), only minor differences become evident, whiles the majority of peaks are of the same energy (e.g. the present peaks at 1614, 1513, 1499, 1469, 1163, 1034, 927, 777 or 529 cm^{-1} may be found also in the spectra of D3). Taken into consideration, the applicant himself appears to admit a certain level of uncertainty of IR-bands (cf. "... having inter alia" in claim 1) and their frequencies (cf. "± 4 cm^{-1}" in claim 1), the novelty of the presently claimed paroxetine salt may at present not be acknowledged.

3.3 Hence, in order that the above difference from the spectra obtained in nujol and KBr could be considered as being meaningful a **direct comparison of the present compound and the compound(s) disclosed in D3** would be required. Accordingly, the applicant is requested to submit suitable data, preferably showing the IR-spectra of either species alone and in admixture with each other, such as described under "infrared (IR) measurements" on page 136ff of D4. Should the applicant fail to provide data, which unambiguously proof the novelty of the claimed subject-matter, oral proceedings under Art. 116(1) EPC will take place upon your request dated 23.12.99.

Haringer